Applicant : Tetsuo Kojima et al.   Attorney's Docket No.: 14875-135US1 / C1-A0204P-US
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Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Previously presented) A method of screening for agonistic antibodies that comprises the following steps (a) to (c):

(a) providing a cell that expresses both a multimer-forming receptor and a test antibody, wherein the cell grow depending on the corresponding ligand of the receptor;

(b) determining the test antibody to comprise agonistic activity when autocrine cell growth is autonomous; and

(c) selecting those antibodies as that comprise agonistic activity.

2. (Original) The method of claim 1, that further comprises the step of introducing a gene that encodes the heavy chain of the test antibody, into the cell of step (a) having been introduced with a gene that encodes the light chain of the test antibody, and a gene that encodes the receptor.

3. (Previously presented) The method of claim 1 wherein the receptor is a chimeric receptor with a protein that comprises a function of transducing a cell growth signal.

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4. (Previously presented) The method of claim 1 wherein the receptor is a dimer-forming receptor.

5. (Previously presented) The method of claim 4 wherein the dimer-forming receptor is a homo-dimer.

6. (Previously presented) The method of claim 4 wherein the dimer-forming receptor is a hetero-dimer.

7. (Previously presented) The method of claim 1 wherein the protein that comprises the function of transducing a cell growth signal is a G-CSF receptor.

8. (Previously presented) The method of claim 1 that comprises the introduction of an antibody library to the cell.

9. (Previously presented) The method of claim 8 wherein the antibody library is a retroviral antibody library.

10. (Previously presented) The method of claim 1 wherein the test antibody is a multi-specific antibody.

11. (Original) The method of claim 10 that comprises linking the test antibody's heavy and light chain variable regions with a linker.

12. (Original) The method of claim 11 that comprises producing the antibody with variable regions linked by a linker, using a method that comprises the steps (a) to (c):

(a) producing a single chain Fv against the first receptor chain;

(b) producing a single chain antibody against the first receptor chain by linking the single chain Fv with a CH1-hinge-CH2-CH3; and

(c) producing a multi-specific antibody that comprises the single chain antibody produced in step (b).

13. (Original) The method of claim 11 that comprises producing the antibody with its variable regions linked by a linker, using a method that comprises the steps (a) to (c):

(a) producing a single chain Fab against the first receptor chain;

(b) producing a single chain antibody against the first receptor chain by linking the single chain Fab with an Fc; and

(c) producing a multi-specific antibody that comprises the single chain antibody produced in step (b).

14-34. (Canceled)

35. (New) A method of screening for agonistic antibodies, the method comprising:

(a) providing a cell that expresses both a multimer-forming receptor and a test antibody, wherein the cell in the absence of the antibody requires a ligand of the receptor for growth;

(b) culturing the cell in the absence of the ligand; and

(c) selecting the test antibody as an agonist of the receptor if the cell grows in the absence of the ligand.

36. (New) The method of claim 35, further comprising the steps of (i) providing a first cell comprising a nucleic acid encoding the light chain of the antibody and a nucleic acid encoding the receptor; and (ii) introducing into the first cell a nucleic acid that encodes the heavy chain of the test antibody, thereby producing the cell of step (a) .

37. (New) The method of claim 35, wherein the receptor is a chimeric receptor that functions to transduce a cell growth signal.

38. (New) The method of claim 35, wherein the receptor is a dimer-forming receptor.

39. (New) The method of claim 38, wherein the dimer-forming receptor is a homo-dimer-forming receptor.

40. (New) The method of claim 38, wherein the dimer-forming receptor is a hetero-dimer-forming receptor.

41. (New) The method of claim 35, wherein the receptor is a G-CSF receptor.

42. (New) The method of claim 35, further comprising a step of producing a plurality of cells expressing a library of diverse antibodies, the cell of step (a) being a member of the plurality of cells.

43. (New) The method of claim 42, wherein the library of diverse antibodies is encoded by a retroviral antibody library introduced into the plurality of cells.

44. (New) The method of claim 35, wherein the test antibody is a multi-specific antibody.

45. (New) The method of claim 44, wherein the test antibody comprises heavy and light chain variable regions connected via a linker.

46. (New) The method of claim 45, further comprising producing the test antibody by a method that comprises:

(i) producing a first DNA encoding a single chain Fv that binds to the receptor;

(ii) producing a second DNA encoding a single chain antibody comprising the single chain Fv of step (i) linked to a CH1-hinge-CH2-CH3; and

(iii) producing a multi-specific antibody that comprises the single chain antibody of step (ii).

47. (New) The method of claim 45, further comprising producing the test antibody by a method that comprises:

(i) producing a first DNA encoding a single chain Fab that binds to the receptor;

(ii) producing a second DNA encoding a single chain antibody comprising the single chain Fab of step (i) linked to an Fc; and

(iii) producing a multi-specific antibody that comprises the single chain antibody of step (ii).

48. (New) A method of screening for agonistic antibodies, the method comprising:

providing an antibody expression library of cells, the cells each expressing both a member of a set of diverse antibodies and a multimer-forming receptor, wherein the cells in the absence of the antibodies require a ligand of the receptor for cell growth;

culturing the library of cells in the absence of the ligand;

selecting a cell that grows in the absence of the ligand; and

identifying the antibody expressed by the selected cell as being an agonist of the receptor.

49. (New) The method of claim 48, wherein the antibody expression library comprises a retroviral antibody library.